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From: Gambel, Phillip
Sent: Wednesday, October 04, 2000 3:09 PM
To: STIC-ILL
Subject: spitler and prostate

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please provide the following references to

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ngl - QR180. I452

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2. salgaller et al. immunological investigations 29 (2) : page 195 (may 2000)
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4. tjoa et al. prostate 40 (2) : 125 - `129 (!999)
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9. tjoa et al. urologic clinics of north america 26 / 2 : 365 - 374 (1999)
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thanx

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IMMUNOLOGICAL INVESTIGATIONS, 29(2), 195 (2000)

1.

PSA TRANSFECTED TUMOR XENOGRAFT PROGRESSION CAN BE MONITORED BY QUANTIFYING PSA IN THE SERUM OF SCID MICE. Thomas F. Conway Jr.*, Michael S. Sabel+ Masahiko Sugano, John G. Frelinger+, Nejat K. Egilmez, Fang-An Chen and Richard B. Bankert, Department of Immunology and +Department of Surgery Roswell Park Cancer Institute, Buffalo, NY, and +University of Rochester, School of Medicine and Dentistry, Rochester, NY

The accurate measurement of the response of a tumor to be given treatment is critical to evaluating novel therapeutic modalities. An experiment design is reported here that can be generally applied to monitoring human tumor xenografts growing in immunodeficient mice. A human non-small cell lung tumor cell line was transfected with a mammalian expression vector containing the gene encoding human prostate specific antigen (PSA) and has been shown to grow progressively following the subcutaneous, intraperitoneal and intravenous inoculation of the tumor into severe combined immunodeficient (SCID) mice. The transfected human tumor cells produce PSA that is detectable in the sera of all tumor inoculated SCID mice. Over a five week period the serum levels of PSA of mice inoculated subcutaneously or intraperitoneally with the tumor increase progressively, and the estimated tumor volumes correlate with the amount of PSA detected in the serum. Serum PSA levels drop rapidly following the surgical debulking of tumor xenograft, reaching background levels of PSA in the serum one week after tumor removal. Serum PSA levels were also observed in SCID mice inoculated intravenously with a PSA transfected human lung tumor cell line adapted to grow orthotopically in the lung. These data establish an experimental design that provides a reliable, non-invasive, accurate and simple approach to monitor and quantify the growth of human tumor xenografts in SCID mice.

2.

ASSESSING THE IMMUNE STATUS OF PROSTATE CANCER PATIENTS INFUSED WITH DENDRITIC CELLS EXPRESSING PSMA-DERIVED PEPTIDES. M. L. Salgaller, L. A. Jones, P. A. Lodge, H. J. Kelley, R. R. Bader, A. L. Boynton, and G. P. Murphy. Northwest Biotherapeutics, Inc., and Pacific Northwest Cancer Foundation, Seattle, WA 98125

In a phase II study, prostate cancer patients with either locally recurrent or metastatic disease were infused with our vaccine: 6 infusions at 6-week intervals using autologous DCs exogenously pulsed with the PSMA-derived peptides, PSM-P1 and -P2. The achievement of several clinical responders permitted us to demonstrate an association between clinical outcome and certain measurements of immunocompetence. Pre-treatment, durable delayed-typed hypersensitivity responses to a panel of recall antigens correlated with response to treatment. Cytokine secretion by PBMC following CD3 cross-linking also correlated with therapeutic benefit. Immunogen-specific cytokine secretion and lytic activity showed no such correlation. Molecular analysis of T cells for factors involved with antigen processing and presentation seem to indicate that it was not responsible for the overall hyporesponsiveness observed with those who showed progressive disease. Thus, when actual clinical responders could be monitored, the functionality of a patient's immune system prior to treatment was the best determinant of outcome. Monitoring could be used an inclusion/exclusion criteria, helping assess which patients are more likely to benefit from a given immunotherapeutic approach.